

REMARKS

Claims 2-32 are pending. Claims 2-27 and 31 are hereby cancelled without prejudice or disclaimer. New claim 33 has been added. Support for the new claim may be found in original claim 31 and in the Specification beginning at page 31, line 33, ending on page 32, line 17, and page 33, lines 1-6.

Applicants submit that no new matter has been added by the amendment to the claims. Applicants also confirm that inventorship has not been changed by the claim amendments.

Claim Objection:

Claims 4-20 have been objected to because they depend from canceled claim 1. Applicants respectfully submit that claims 4-20 have been canceled herein making the objection moot. Applicants request reconsideration and withdrawal of the objection.

Claims 12, 15, and 16 have been objected to because the additional method step is out of order. Applicants respectfully submit that claims 12, 15, and 16 have been canceled herein making the objection moot. Applicants request reconsideration and withdrawal of the objection.

In light of the foregoing argument, Applicants respectfully request the reconsideration and withdrawal of the objections to the claims.

Claim Rejections:

35 USC §112, second paragraph:

Claims 1-21 have been rejected under 35 USC §112, second paragraph as being indefinite. Claims 1-21 have been canceled by this Amendment making the rejection moot.

35 USC §112, first paragraph:

Claims 17-21 have been rejected under 35 USC §112, first paragraph as failing to comply with the written description requirement. Without admitting the propriety of the rejection, Claims 17-21 have been canceled by this Amendment making the rejection moot.

35 USC §102(b):

Claims 21-26 have been rejected under 35 USC §102(b) as being anticipated by Hardman (US Patent No. 4,939,666, issued July 3, 1990). Without admitting the propriety of the rejection, Applicants submit that claims 21-26 have been canceled by this Amendment making the rejection of the claims moot.

Applicants respectfully request reconsideration and withdrawal of the rejection of the above-claims.

35 USC §103:

Claim 29 has been rejected under 35 USC §103(a) as being unpatentable over Hardman (US Patent No. 4,939,666, issued July 3, 1990) in view of Lee et al. (US Patent No. 5,241,470, issued August 31, 1993).

Hardman (US Patent No. 4,939,666, issued July 3, 1990) discloses a method constructing a polypeptide chain having a substantially predetermined conformation. The method incrementally constructs macromolecules starting with a known stable well-mapped polypeptide structure and incrementally adding peptide blocks, based on a library of oligopeptide units having precomputed parameters for each block. (See the Abstract).

Further, Hardman modifies the backbone but does not change the sequence in the optimization step. In other words, Hardman is attempting to achieve a local optimum in a structural space using a fixed sequence. Hardman does not teach or suggest the use of a forcefield calculation in his method.

Lee et al. discloses a method of determining the three-dimensional structure of a peptide having amino acid side chains extending from a defined main chain backbone, each amino acid having predefined rotational degrees of freedom. (See the Abstract). Lee does not teach or suggest the use of different amino acid side chains at any position; rather, Lee is interested in finding the lowest energy conformation of a particular sequence. Lee also does not teach or suggest the use of a forcefield calculation

In contrast, the Applicants' method utilizes a forcefield calculation, among other potential scoring functions, to create optimized sequences from among a plurality of possible sequences in light of the desired folded structure; thus, it is a sequence optimization technique, rather than a conformational optimization of a particular sequence, such as Hardman and Lee.

In a *prima facie* case of obviousness, three criteria must be met: i) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; ii) there must be a reasonable expectation of success; and iii) the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's

disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) M.P.E.P. §2143.

As to the first factor, there is no motivation to combine. Lee relies on a fixed sequence analysis, and Hardman relies on the addition of fixed sequence building blocks to an existing sequence. There simply is no motivation to combine the two. The Examiner states that one of skill in the art would be motivated to combine these references so as to be able to test the accuracy of the three-dimensional protein structure prediction as produced by Hardman. However, Hardman already has a method for testing the accuracy of the structure, so no motivation exists.

Furthermore, Applicants submit that there is no reasonable expectation of success because combining Hardman with Lee destroys the teachings of Hardman or alternatively, of Lee. As to Hardman, This is because Lee's method is based on a "fixed" backbone side chain structure, resulting in a single sequence, while Hardman incrementally builds up existing structures to make a new backbone. Therefore, although Hardman utilizes a computerized methodology, the two methods are not compatible and do not teach the Applicants' invention.

Finally, Applicants submit that neither Hardman nor Lee discloses, teaches or suggests each and every limitation of the claims. Neither Hardman nor Lee teach or suggest the consideration of multiple amino acid side chains in a particular position, nor of the use of forcefield calculations.

Applicants respectfully request the rejection of Claim 29 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Double Patenting:

With respect to claims 29 and 31, claim 31 has been canceled thereby making an objection under 37 CFR 1.75 moot. Claims 2-27 and 31 have been canceled making all non-statutory double patenting rejections moot with respect to these claims. Claims 30 and 32 have been provisionally rejected under obviousness-type double patenting as being upatentable over claims 29-37, 39-48, 29 and 32 of co-pending US Application No. 09/837,886. Claims 30 and 32 have been provisionally rejected as being verbatim and identical in scope to claims 30-37 and 39-48 of the '886 application. Claims 28 and 29 have been provisionally rejected under obviousness-type double patenting as being upatentable over claim 6 of US Patent No. 6,188,965, issued February 31, 2001.

Without admitting the propriety of the rejection, a terminal disclaimer is enclosed. Therefore, the obvious-type double patenting rejection has been made moot. Applicants respectfully request reconsideration and withdrawal of the obviousness-type double patenting rejection based on US Patent No. 6,188,965 and co-pending US Application No. 09/837,886.

The Applicants submit that in light of the above-amendment and argument submission of a terminal disclaimer, the claims are now in condition for allowance and an early notification of such is respectfully solicited.

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Dated: January 15, 2004

Respectfully Submitted,

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